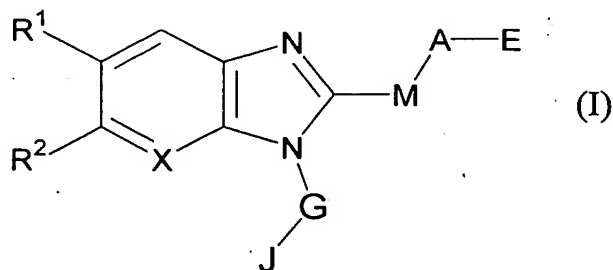


## CLAIMS

1. A drug for improving glucose intolerance comprising a chymase inhibitor as an active ingredient.
2. A preventive drug and/or therapeutic drug of diseases caused by glucose intolerance comprising a chymase inhibitor as an active ingredient.
3. A preventive and/or therapeutic drug according to claim 2 wherein the diseases caused by glucose intolerance are diabetes and/or diabetes complications.
4. A preventive and/or therapeutic drug according to claim 3 wherein the diabetes complications are diabetic nephropathy, diabetic retinopathy, diabetic peripheral neuropathy, hyperinsulinism, insulin resistance syndrome, arteriosclerosis, acute coronary syndrome, arteriosclerosis obliterans, angitis, stroke, hypertension, renal insufficiency, nephropathy, nephritis, renal artery aneurysm, renal infarction or obesity.
5. A preventive and/or therapeutic drug according to claim 3 wherein the diabetes complications are diabetic nephropathy, diabetic retinopathy or diabetic peripheral neuropathy.
6. A drug described according to any of claims 1–5 containing a chymase inhibitor at an amount sufficient for improving glucose intolerance.
7. A drug described in any of claims 1–6 comprising an ACE inhibitor.
8. A drug described according to any of claims 1–7 wherein the chymase inhibitor is the compound represented by formula (I):



[wherein  $R^1$  and  $R^2$  simultaneously or each independently represent hydrogen, halogen, trihalomethyl, cyano, hydroxyl,  $C_1$ – $C_4$  alkyl or  $C_1$ – $C_4$  alkoxy, or  $R^1$  and  $R^2$  taken together represent  $-O-CH_2-O-$ ,  $-O-CH_2CH_2-O-$  or  $-CH_2CH_2CH_2-$ , (wherein the carbon atoms may

be optionally substituted by one or more  $C_1-C_4$  alkyl);

A represents substituted or unsubstituted straight, cyclic or branched  $C_1-C_7$  alkylene or alkenylene, which may be interrupted by one or more of atoms or groups selected from  $-O-$ ,  $-S-$ ,  $-SO_2-$  and  $-NR^3-$  (wherein  $R^3$  represents hydrogen or straight or branched  $C_1-C_6$  alkyl), the substituents on these groups being selected from halogen, hydroxyl, nitro, cyano, straight or branched  $C_1-C_6$  alkyl, straight or branched  $C_1-C_6$  alkoxy (including cases wherein the neighboring two form an acetal), straight or branched  $C_1-C_6$  alkylthio, straight or branched  $C_1-C_6$  alkylsulfonyl, straight or branched  $C_1-C_6$  acyl, straight or branched  $C_1-C_6$  acylamino, trihalomethyl, trihalomethoxy, phenyl, oxo or phenoxy optionally substituted with one or more halogen atoms, wherein one or more of these substituents may each independently be present at any position in the alkylene or alkenylene, except for the case wherein M represents a single bond and the carbon atom of A directly bonded to M is substituted with a hydroxyl and a phenyl at the same time;

E represents  $-COOR^3$ ,  $-SO_3R^3$ ,  $-CONHR^3$ ,  $-SO_2NHR^3$ , tetrazol-5-yl, 5-oxo-1,2,4-oxadiazol-3-yl or 5-oxo-1,2,4-thiadiazol-3-yl, (wherein  $R^3$  is as defined above);

G represents substituted or unsubstituted straight or branched  $C_1-C_6$  alkylene, which may be interrupted by one or more of atoms or groups selected from  $-O-$ ,  $-S-$ ,  $-SO_2-$  and  $-NR^3-$  (wherein  $R^3$  is as defined above, provided that either of these atoms or groups is not directly attached to the benzimidazole ring), the substituents on the said alkylene being selected from halogen, hydroxyl, nitro, cyano, straight or branched  $C_1-C_6$  alkyl, straight or branched  $C_1-C_6$  alkoxy (including cases wherein neighboring two form an acetal), trihalomethyl, trihalomethoxy, phenyl or oxo;

M represents a single bond or  $-S(O)_m-$ , wherein m is an integer ranging from 0 to 2;

J represents substituted or unsubstituted  $C_4-C_{10}$  heteroaryl (one or more heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur in the ring), except for imidazole or unsubstituted pyridine ring, the substituents on the said heteroaryl are halogen, hydroxyl, nitro, cyano, straight or branched  $C_1-C_6$  alkyl, straight or branched  $C_1-C_6$  alkoxy (including cases wherein neighboring two form an acetal), straight or branched  $C_1-C_6$  alkylthio, straight or branched  $C_1-C_6$  alkylsulfonyl, straight or branched  $C_1-C_6$  acyl, straight or branched

C<sub>1</sub>–C<sub>6</sub> acylamino, substituted or unsubstituted anilido, trihalomethyl, trihalomethoxy, phenyl, oxo, COOR<sup>3</sup> or phenoxy optionally substituted with one or more halogen atoms, wherein one or more of these substituents may each independently be present at any position in the ring; and X represents –CH= or nitrogen].

9. A drug according to claim 8 wherein, in formula (I), R<sup>1</sup> and R<sup>2</sup> are simultaneously or each independently hydrogen, C<sub>1</sub>–C<sub>4</sub> alkyl, C<sub>1</sub>–C<sub>4</sub> alkoxy, halogen or cyano;

A is n-propylene;

E is –COOH;

G is methylene;

M is –S–;

J is substituted or unsubstituted benzothienyl or indolyl (wherein the substituent is halogen, hydroxyl, nitro, cyano, straight or branched C<sub>1</sub>–C<sub>6</sub> alkyl, straight or branched C<sub>1</sub>–C<sub>6</sub> alkoxy (including cases wherein neighboring two form an acetal), straight or branched C<sub>1</sub>–C<sub>6</sub> alkylthio, straight or branched C<sub>1</sub>–C<sub>6</sub> alkylsulfonyl, straight or branched C<sub>1</sub>–C<sub>6</sub> acyl, straight or branched C<sub>1</sub>–C<sub>6</sub> acylamino, substituted or unsubstituted anilido, trihalomethyl, trihalomethoxy, phenyl, oxo, COOR<sup>3</sup> or phenoxy optionally substituted with one or more halogen atoms, wherein one or more of these substituents may each independently be present at any position in the ring);

and

X is –CH=.

10. A drug according to claim 8 or 9 wherein R<sup>1</sup> and R<sup>2</sup> are simultaneously or each independently hydrogen, C<sub>1</sub>–C<sub>4</sub> alkyl or C<sub>1</sub>–C<sub>4</sub> alkoxy.

11. A drug according to claim 10 wherein R<sup>1</sup> and R<sup>2</sup> are simultaneously or each independently hydrogen, methyl or methoxy.

12. A drug according to any of claims 8–11 wherein J is benzothienyl.

13. A drug according to any of claims 8–12 wherein the substituent on J is halogen, cyano, straight or branched C<sub>1</sub>–C<sub>4</sub> alkyl, straight or branched C<sub>1</sub>–C<sub>4</sub> alkoxy (including cases wherein neighboring two form an acetal) or trihalomethyl.

14. A drug according to claim 13 wherein the substituent on J is F, Cl, cyano, methyl, methoxy or trifluoromethyl.

15. A drug according to claim 14 wherein the substituent on J is methyl.
16. A drug according to any of claims 1–7 wherein the chymase inhibitor is
  - 4-(1-((3-indolyl)methyl)benzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((3-benzo[b]thienyl)methyl)-5-methoxybenzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((5-methylbenzo[b]thiophen-3-yl)methyl)-5-methoxybenzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((4-methylbenzo[b]thiophen-3-yl)methyl)-5-methoxybenzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((3-benzo[b]thienyl)methyl)-5-cyanobenzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((5-methylbenzo[b]thiophen-3-yl)methyl)-6-methoxybenzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((4-methylbenzo[b]thiophen-3-yl)methyl)-6-methoxybenzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((1,5-dimethylindol-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((1-methyl-4-chloroindol-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((1-methyl-4-fluoroindol-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((5-chlorobenzo[b]thiophen-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((5-methylbenzo[b]thiophen-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((4-methylbenzo[b]thiophen-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((4-chlorobenzo[b]thiophen-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((4,6-dimethylbenzo[b]thiophen-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((1-methylindol-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((1,4-dimethylindol-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((1-methyl-4-chloroindol-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((benzo[b]thiophen-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((5-chlorobenzo[b]thiophen-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid,
  - 4-(1-((5-methylbenzo[b]thiophen-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid,

4-(1-((4-methylbenzo[b]thiophen-3-yl)methyl)-5,6-dimethylbenzimidazol-2-ylthio)butanoic acid,

4-(1-((1,4-dimethylindol-3-yl)methyl)-5,6-dichlorobenzimidazol-2-ylthio)butanoic acid,

4-(1-((benzo[b]thiophen-3-yl)methyl)-5,6-dichlorobenzimidazol-2-ylthio)butanoic acid,

4-(1-((benzo[b]thiophen-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid,

4-(1-((benzo[b]thiophen-3-yl)methyl)-5-methylbenzimidazol-2-ylthio)butanoic acid,

4-(1-((benzo[b]thiophen-3-yl)methyl)-6-methylbenzimidazol-2-ylthio)butanoic acid,

4-(1-((1,4-dimethylindol-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid,

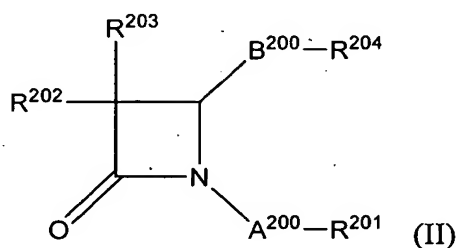
4-(1-((1,4-dimethylindol-3-yl)methyl)-5-methoxybenzimidazol-2-ylthio)butanoic acid or

4-(1-((1-methyl-4-chloroindol-3-yl)methyl)-5-methoxybenzimidazol-2-ylthio)butanoic acid.

17. A drug according to any of claims 1–7 wherein the chymase inhibitor is

4-(1-((4-methylbenzo[b]thiophen-3-yl)methyl)benzimidazol-2-ylthio)butanoic acid.

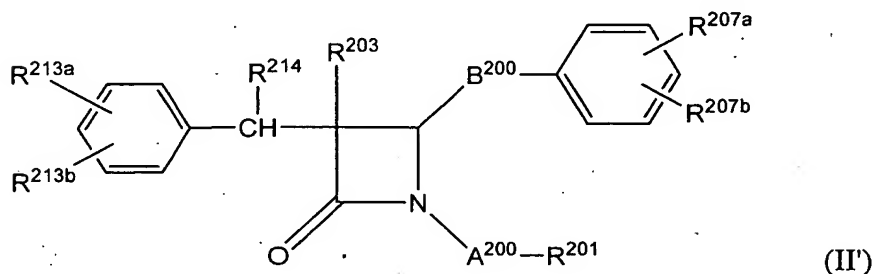
18. A drug described in any of claims 1–7 wherein the chymase inhibitor is the compound represented by formula (II), a prodrug, a pharmaceutically acceptable salt thereof or a hydrate thereof:



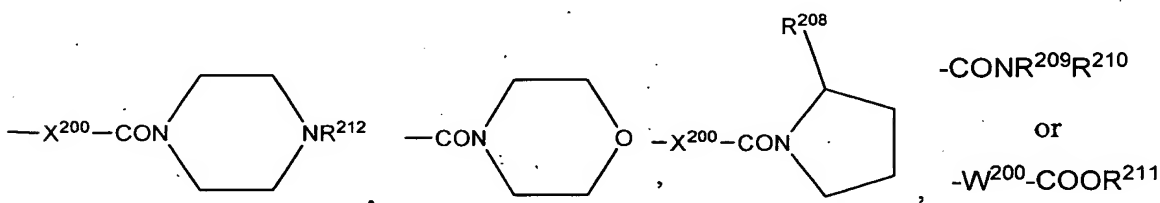
[wherein  $A^{200}$  represents a single bond,  $-CO-$ ,  $-COO-$ ,  $-COCO-$ ,  $-CONH-$  or  $-SO_2-$ ,  $R^{201}$  represents lower alkyl optionally having substituents, lower alkenyl optionally having substituents, lower alkynyl optionally having substituents, cycloalkyl optionally having substituents, cycloalkenyl optionally having substituents or aryl optionally having substituents,  $R^{201}$  may be hydrogen when  $A^{200}$  is a single bond,  $-CO-$ ,  $-COCO-$ ,  $-CONH-$  or  $-SO_2-$ ,  $R^{202}$  and  $R^{203}$  are each independently hydrogen, halogen, lower alkyl optionally having substituents, lower alkoxy carbonyl optionally having substituents, acyl optionally having substituents, amino optionally having substituents, carbamoyl optionally having substituents or aryl optionally having substituents,  $B^{200}$  represents a single bond,  $-S-$ ,  $-O-$ ,  $-S-S-$ ,  $-SO-$  or  $-SO_2-$ ,

$R^{204}$  represents hydrogen, lower alkyl optionally having substituents, aryl optionally having substituents or heterocyclyl optionally having substituents, and  $R^{204}$  may be acyl optionally having substituents when  $B^{200}$  is a single bond,  $-S-$ ,  $-O-$ ,  $-SO-$  or  $-SO_2-$ ].

19. A drug of claim 18 wherein the chymase inhibitor is the compound represented by formula (II'), a prodrug, a pharmaceutically acceptable salt thereof or a hydrate thereof:



(wherein  $A^{200}$  and  $R^{201}$  are as defined for formula (II),  $R^{203}$  represents hydrogen, halogen, lower alkoxy carbonyl optionally having substituents, acyl optionally having substituents, amino optionally having substituents, aryl optionally having substituents or benzyl optionally having substituents,  $R^{213a}$  and  $R^{213b}$  each independently represent hydrogen, halogen, hydroxyl, lower alkyl optionally having substituents, lower alkoxy optionally having substituents, amino optionally having substituents or lower alkylthio optionally having substituents, or  $R^{213a}$  and  $R^{213b}$  taken together form lower alkylenedioxy,  $R^{214}$  represents hydrogen, hydroxyl, lower alkyl, lower alkoxy or acyloxy,  $R^{207a}$  represents hydrogen,



(wherein  $X^{200}$  and  $W^{200}$  represent a single bond, methylene or vinylene,  $R^{208}$  represents methyl or carbamoyl,  $R^{209}$  represents hydrogen or lower alkyl,  $R^{210}$  represents lower alkyl optionally having substituents (lower alkylamino; phenyl optionally substituted with halogen; carboxyl; or lower alkoxy carbonyl optionally substituted with aryl), lower alkenyl, lower alkylamino, phenylamino, phenyl or benzenesulfonyl,  $R^{211}$  represents hydrogen or lower alkyl optionally having substituents (lower alkylamino; acyloxy; phenyl optionally substituted with halogen or

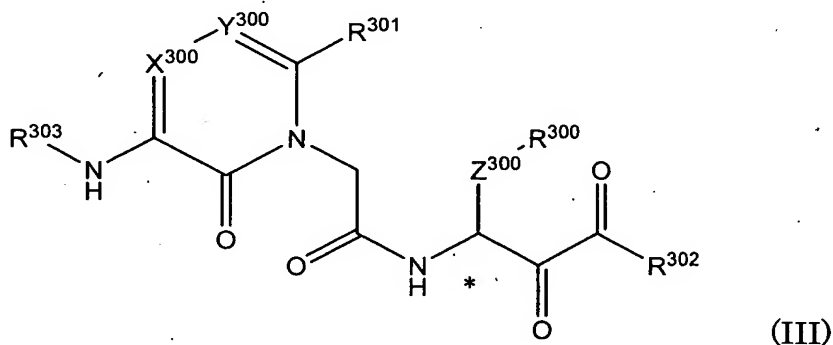
methylenedioxy; or heterocyclyl) and  $R^{212}$  represents  $C_1$ – $C_3$  alkyl or cyclohexyl),  $R^{207b}$  is hydrogen, and  $B^{200}$  is O or S).

20. A drug according to claim 18 wherein the chymase inhibitor is

4-[1-[N-[bis(4-methylphenyl)methyl]carbamoyl]-3-(2-ethoxybenzyl)-4-oxoazetidin-2-yloxy] benzoic acid or

4-[1-[(bis(4-methoxyphenyl)methyl]carbamoyl]-3-(2-ethoxybenzyl)-4-oxoazetidin-2-yloxy] benzoic acid, a prodrug, a pharmaceutically acceptable salt thereof or a hydrate thereof.

21. A drug according to any of claims 1–7 wherein the chymase inhibitor is the novel acetamide derivative represented by formula (III) below or a pharmaceutically acceptable salt thereof:



[wherein  $R^{300}$  is phenyl, which may have one or more substituents selected from group  $A^{300}$  defined below (wherein  $A^{300}$  is halogen, nitro, hydroxyl, lower alkoxy, lower alkyl or halogenated lower alkyl);

$R^{301}$  is (III-i) aryl, (III-ii) heteroaryl or (III-iii) straight, branched or cyclic  $C_1$ – $C_6$  alkyl and may have each independently one or more substituents selected from group  $A^{300}$ ; or  $R^{301}$  may have, on group (III-i) – (III-iii), one or more substituents selected from group  $B^{300}$ , consisting of  $OR^{300a}$ ,  $COOR^{300a}$ ,  $CONR^{300b}R^{300c}$ ,  $NR^{300b}R^{300c}$ ,  $NR^{300b}CHO$ ,  $NR^{300b}COR^{300a}$ ,  $SO_2OR^{300a}$ ,  $SO_2R^{300a}$ ,  $CONR^{300b}SO_2R^{300a}$  and  $P(O)(OR^{300a})_2$  (wherein,  $R^{300a}$ – $R^{300c}$  are independently hydrogen, lower alkyl or substituted lower alkyl; or  $R^{300a}$ – $R^{300c}$  are independently aryl( $C_1$ – $C_7$ )alkyl, heteroaryl( $C_1$ – $C_7$ )alkyl, aryl or heteroaryl wherein the ring of aryl or heteroaryl may have one or more, usually one to three substituents selected from group A and the lower alkyl has one to three substituents selected from halogen, nitro and hydroxyl); or  $R^{301}$  may have on group (III-i) – (III-iii) one or more substituents selected from cyclic group  $G^{300}$ ,

(wherein  $G^{300}$  represents five- or six-membered heterocyclcyl having one to three oxygen or nitrogen and optionally have substituents);

$R^{302}$  is  $C_1-C_8$  alkyl, aryl( $C_1-C_7$ )alkyl, heteroaryl( $C_1-C_7$ )alkyl or aryl; or  $R^{302}$  is group  $B^{300}$  defined above,  $C_1-C_8$  alkyl substituted with group  $B^{300}$  or  $C_1-C_8$  alkyl substituted with cyclic group  $G^{300}$  defined above;

$R^{303}$  is hydrogen; or  $R^{303}$  is acyl represented by (i)  $D^{300}(CH_2)_{0-3}CO$ , (ii)  $D^{300}COE^{300}CO$  or (iii)  $D^{300}SO_2E^{300}CO$ ; or  $R^3$  is sulfonyl represented by  $D^{300}(CH_2)_{0-3}SO_2$  or  $D^{300}COE^{300}SO_2$  (wherein group  $D^{300}$  is hydrogen, straight, branched or cyclic  $C_1-C_6$  alkyl, aryl, halogenated lower alkyl, halogenated lower alkoxy, amino, lower alkoxyamino, halogenated lower alkylamino,  $R^{300b}R^{300c}N$ ,  $R^{300b}R^{300c}NO$ ,  $R^{300a}O$ ,  $R^{300a}$ ,  $R^{300a}OCO$ ,  $R^{300b}R^{300c}NCO$ ,  $R^{300a}SO_2NR^{300b}$ ,  $R^{300a}S$ , or cyclic group  $G^{300}$  as defined above, and group  $E^{300}$  represents divalent bridging group having 1 to 6 carbon atoms); or  $R^{303}$  is urea represented by  $R^{300b}R^{300c}NCO$ ; or  $R^{303}$  is thiourea represented by  $R^{300b}R^{300c}NCS$ ; or  $R^{303}$  is  $R^{303a}$ ;

$X^{300}$  and  $Y^{300}$  each represent independently nitrogen or carbon and may be substituted with a group represented by  $R^{300a}-R^{300c}$ ; and

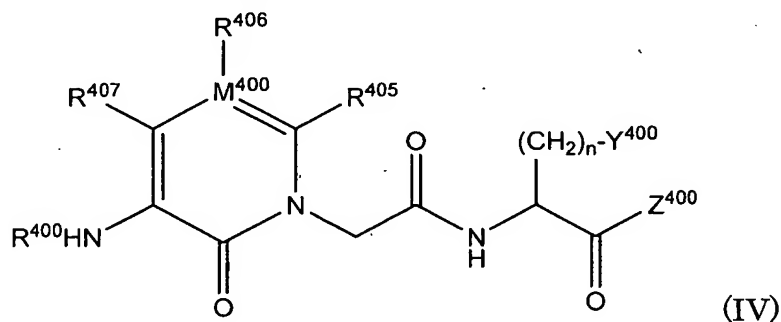
$Z^{300}$  is polymethylene wherein each hydrogen may independently be substituted with  $R^{300a}$  or  $R^{300b}$ ].

22. A drug according to claim 21 wherein  $R^{300}$  is unsubstituted phenyl,  $R^{301}$  is unsubstituted phenyl,  $R^{302}$  is unsubstituted  $C_1-C_8$  alkyl or  $C_1-C_8$  alkyl having substituents selected from pyrrolidin-1-yl, pyridyloxy, 2-oxo-1,2-dihydropyridin-1-yl, pyrimidyloxy, pirazyloxy, pyridazyloxy, lower alkyl-substituted piperazin-1-yl or lower alkyl-substituted piperazin-1-ylcarbonyl, X is unsubstituted carbon, Y is nitrogen and Z is  $-CH_2-$ .

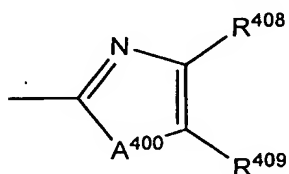
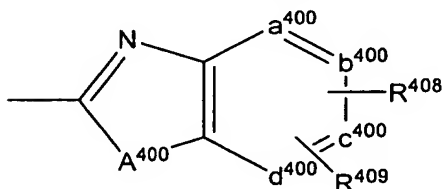
23. A drug according to claim 21 wherein the chymase inhibitor is 2-(5-substituted-6-oxo-2-phenyl-1,6-dihydropyrimidin-1-yl)-N-{2,3-dioxo-6-(2-pyridyloxy)-1-phenylmethyl}hexylacetamide wherein the substituent is amino, t-butyloxycarbonylamino, benzylsulfonylamino, formylamino, benzylaminosulfonylamino, 4-pyridylmethyloxycarbonylamino or acetylamino, or N-[1-benzyl-2,3-dioxo-6-(2-pyridyloxy)hexyl]-2-[5-(formylamino)-6-oxo-2-phenyl-1,6-dihydropyrimidin-1-yl]acetamide.

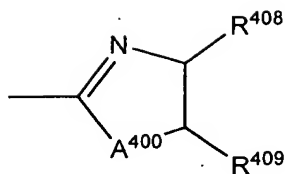


24. A drug described according to any of claims 1-7 wherein the chymase inhibitor is the heterocyclic amide represented by formula (IV) or a pharmacologically acceptable salt thereof:



[wherein  $R^{400}$  is hydrogen, alkyl,  $-\text{CHO}$ ,  $-\text{CONH}_2$ ,  $-\text{COR}^{401}$ ,  $-\text{COOR}^{401}$ ,  $-\text{CONHOR}^{401}$ ,  $-\text{CONHR}^{401}$ ,  $-\text{CONR}^{401}\text{R}^{401'}$ ,  $-\text{CONHSO}_2\text{R}^{401}$ ,  $-\text{COSR}^{401}$ ,  $-\text{COCOR}^{402}$ ,  $-\text{COCOOR}^{402}$ ,  $-\text{CONHCOOR}^{402}$ ,  $-\text{COCONR}^{403}\text{R}^{404}$ ,  $-\text{CSX}^{400}\text{R}^{401}$ ,  $-\text{SO}_2\text{WR}^{401}$ ,  $-\text{SO}_2\text{NR}^{401}\text{R}^{401'}$  or  $-\text{SO}_2\text{E}^{400}$  (wherein  $R^{401}$  and  $R^{401'}$  may be the same or different and each independently represent alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, heterocyclyl or heterocyclylalkyl,  $R^{402}$ ,  $R^{403}$  and  $R^{404}$  may be the same or different and they each independently represent hydrogen, alkyl or arylalkyl, or  $-\text{NR}^{403}\text{R}^{404}$  taken together may represent heterocyclyl,  $X^{400}$  represents a single bond,  $-\text{NH}-$ ,  $-\text{O}-$  or  $-\text{S}-$ ,  $W^{400}$  represents a single bond,  $-\text{NH}-$ ,  $-\text{NHCO}-$ ,  $-\text{NHCOO}-$  or  $-\text{NHCONH}-$ , and  $E^{400}$  represents hydroxyl or amino),  $R^{405}$ ,  $R^{406}$  and  $R^{407}$  may be the same or different, and either they each independently represent hydrogen or alkyl, or one of them represents aryl, arylalkyl, arylalkenyl, heteroaryl, heteroarylalkyl or heteroarylalkenyl with the rest being hydrogen,  $M^{400}$  represents carbon or nitrogen, wherein  $R^{406}$  is absent if  $M^{400}$  is nitrogen,  $Y^{400}$  represents cycloalkyl, aryl or heteroaryl,  $Z^{400}$  represents the groups shown by formula (IV-i), (IV-ii) and (IV-iii):





(IV-iii)

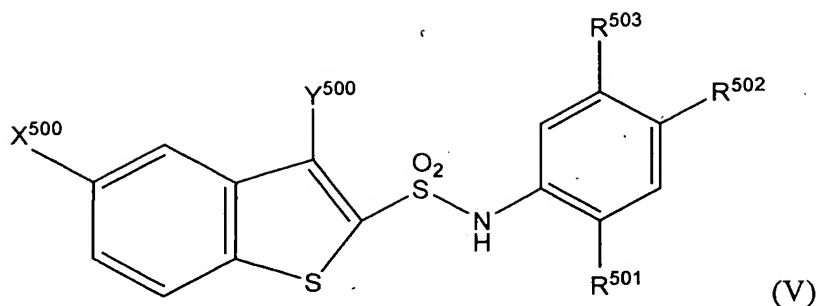
{ wherein,  $R^{408}$  and  $R^{409}$  may be the same or different and they each independently represent hydrogen, alkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, halogen, trifluoromethyl, cyano, nitro,  $-NR^{410}R^{410'}$ ,  $-NHSO_2R^{410}$ ,  $-OR^{410}$ ,  $-COOR^{410}$ ,  $-CONHSO_2R^{410}$  or  $-CONR^{410}R^{410'}$  (wherein  $R^{410}$  and  $R^{410'}$  may be the same or different and they each independently represent hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl or trifluoromethyl, or  $-NR^{410}R^{410'}$  taken together may represent heterocyclyl),  $A^{400}$  represents  $-O-$ ,  $-S-$  or  $-NR^{412}-$  (wherein  $R^{412}$  represents hydrogen, alkyl, cycloalkyl or cycloalkylalkyl),  $a^{400}$ ,  $b^{400}$ ,  $c^{400}$  and  $d^{400}$  are all carbon or one of them is nitrogen with the rest being carbon},  $n$  is 0 or 1; and

among the said groups alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, arylalkenyl, heteroaryl, heteroarylalkyl, heteroarylalkenyl, heterocyclyl and heterocyclylalkyl each may have substituents].

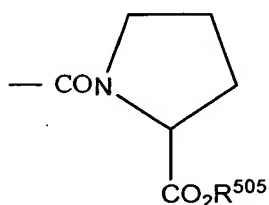
25. A drug according to claim 24 wherein  $Y^{400}$  is aryl optionally having substituents,  $Z^{400}$  is the group represented by formula (IV-i), one of  $R^{405}$ ,  $R^{406}$  and  $R^{407}$  is aryl optionally having substituents with the rest being hydrogen, wherein  $R^{406}$  is absent when  $M$  is nitrogen.

26. A drug according to claim 24 wherein the chymase inhibitor is methyl 2-[2-[2-[5-amino-2-(3-methoxyphenyl)-6-oxo-1,6-dihydropyrimidin-1-yl]acetamido]-3-phenylpropionyl]benzoxazole-5-carboxylate or methyl 2-[2-[5-amino-2-(4-fluorophenyl)-6-oxo-1,6-dihydropyrimidin-1-yl]acetamido]-3-phenylpropionyl]benzoxazole-5-carboxylate.

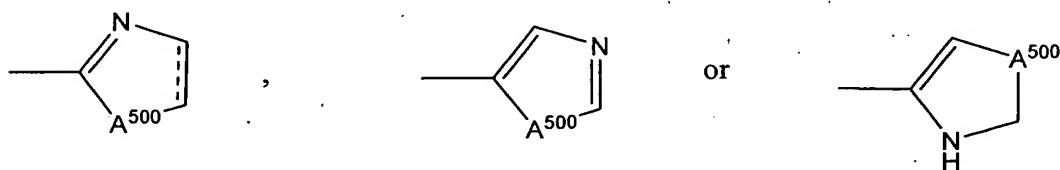
27. A drug according to any of claims 1-7 wherein the chymase inhibitor is the N-substituted benzothiophenesulfonamide derivative represented by formula (V) or a salt thereof:



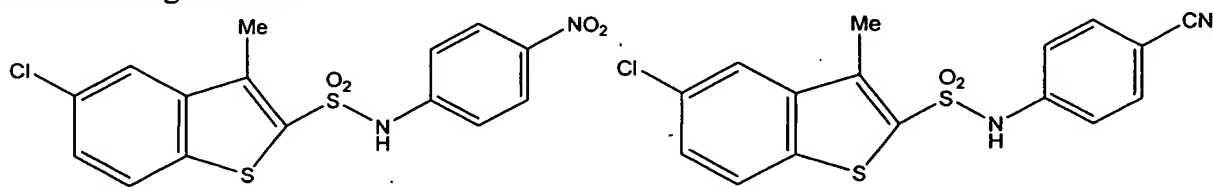
[wherein X<sup>500</sup> represents hydrogen, halogen or lower alkyl, Y<sup>500</sup> represents lower alkyl, R<sup>501</sup> and R<sup>502</sup> each may be the same or different and independently represent hydrogen, lower alkoxy carbonyl, lower alkylsulfonyl, benzoyl, C<sub>1</sub>-C<sub>4</sub> acyl, lower alkoxy, lower alkoxy carbonylmethylthioacetyl, nitro, -CONHR<sup>504</sup> (wherein R<sup>504</sup> represents hydrogen, lower alkoxy carbonylmethyl, carboxymethyl or -CH(CH<sub>2</sub>OH)COOR<sup>505</sup> (wherein R<sup>505</sup> represents hydrogen or lower alkyl)), the group represented by

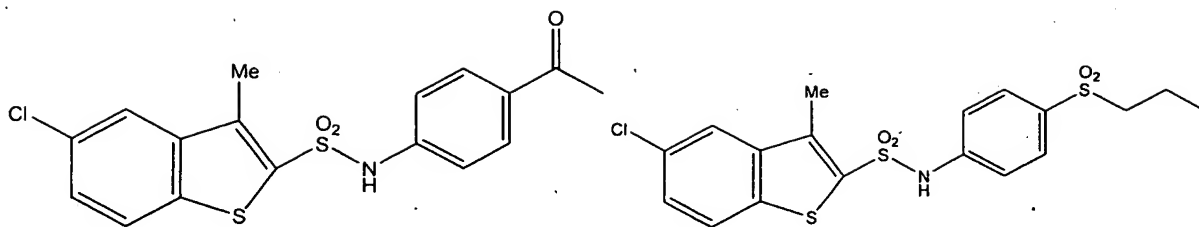


(wherein R<sup>505</sup> is as defined above), the monocyclic heterocyclyl represented by



optionally substituted with  $-\text{CO}_2\text{R}^{505}$  (wherein  $\text{A}^{500}$  represents O, S or NH, the bond accompanying a dotted line represents a single or double bond and  $\text{R}^{505}$  is as defined above), lower hydroxyalkyl or cyano (except for cases wherein both  $\text{R}^{501}$  and  $\text{R}^{502}$  are hydrogen), and  $\text{R}^{503}$  represents hydrogen, lower alkoxy or lower alkyl], excluding compounds represented by the following formulas.





28. A drug according to claim 27 wherein the chymase inhibitor is  
 2-[4-(5-fluoro-3-methylbenzo[b]thiophen-2-yl)sulfonamido-3-methanesulfonylphenyl]  
 oxazole-4-carboxylic acid.